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? show files
File 155:MEDLINE(R) 1966-2003/Mar W1
         (c) format only 2003 The Dialog Corp.
File   5:Biosis Previews(R) 1969-2003/Mar W1
         (c) 2003 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Mar W1
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File  71:ELSEVIER BIOBASE 1994-2003/Mar W1
         (c) 2003  Elsevier Science B.V.
File  73:EMBASE 1974-2003/Mar W1
         (c) 2003 Elsevier Science B.V.
File 144:Pascal 1973-2003/Feb W4
         (c) 2003 INIST/CNRS
File 342:Derwent Patents Citation Indx 1978-01/200254
         (c) 2003 Thomson Derwent
File 351:Derwent WPI 1963-2003/UD,UM &UP=200315
         (c) 2003  Thomson Derwent
File 398:CHEMSEARCH(TM) 1957-2003/Feb
         (c) 2003 Amer.Chem.Soc.
File 440:Current Contents Search(R) 1990-2003/Mar 07
         (c) 2003 Inst for Sci Info
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Set     Items   Description
S1         27   TETRAZOL?)(S)(DECAHYDROISOQUINOLONE OR ISOQUINOL?)(S)(3(W)-
              CARBOXYL?)
S2         21   RD (unique items)
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? t s2/3 ab/1-21
>>>No matching display code(s) found in file(s): 342, 398

 2/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

09844945   98272489   PMID: 9610933
  The putative AMPA receptor antagonist, LY326325, produces anxiolytic-like
effects without altering locomotor activity in rats.
  Kotlinska J; Liljequist S
  Department of Clinical Neuroscience, Karolinska Institute, Stockholm,
Sweden.
  Pharmacology, biochemistry, and behavior (UNITED STATES)  May 1998, 60
 (1) p119-24, ISSN 0091-3057  Journal Code: 0367050
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Anxiolytic-like effects produced by the novel, water-soluble AMPA/kainate
receptor antagonist, LY326325 (3RS,4aRS,6RS,8aRS)-6-[2-(1(2)H-tetrazole-5-y
l)e    thyl]decahydro-isoquinoline-3-carboxylic  acid),  were
examined in the elevated plus-maze and in a conflict-suppressed drinking
situation. Administration of low doses (0.5, 1.2, and 5 mg/kg; i.p., -30
min) of LY326325 to Sprague-Dawley rats did not alter the percentage of
entries into the open arms of the plus-maze, whereas only one dose of
LY326325 (1 mg/kg) produced a slight, but significant, increase of the time
spent in the open arms of the plus maze. In the conflict-suppressed
drinking test, similar doses of LY326325 (2.5 and 5 mg/kg; i.p., -30 min)
caused a dose-dependent and significant increase of punished drinking
behavior without having any significant effects on unpunished drinking. The
anxiolytic-like effects of LY326325 in the plus-maze and in the
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anticonflict tests were observed at doses, which, by themselves, had no influence on various measures of locomotor activity, i.e., horizontal activity, forward locomotion, and corner time. Our data suggest that the putative AMPA/glutamate receptor antagonist, LY326325, produces anxiolytic-like effects similar to those of diazepam in the conflict-suppressed drinking test, but displays considerably weaker anxiety-reducing properties compared to diazepam in the elevated plus-maze.

2/AB/2 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08314341 BIOSIS NO.: 000094076664
THE DISCOVERY AND CHARACTERIZATION OF THE COMPETITIVE NMDA ANTAGONISTS LY274614 LY233536 AND LY233053
AUTHOR: ZIMMERMAN D M; SCHOEPP D D; LEANDER J D; ORNSTEIN P L
AUTHOR ADDRESS: CNS RES. DIV., LILLY RES. LAB., ELI LILLY CO., LILLY CORP. CENT., INDIANAPOLIS, INDIANA 46285.
JOURNAL: MOL NEUROPHARMACOL 2 (1). 1992. 77-81. 1992
CODEN: MOLNE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Based on differences observed in the pharmacology of non-competitive phencyclidine (PCP)-like antagonists and competitive N-methyl-D-aspartate (NMDA) antagonists, we decided to develop the latter as potential therapeutic agents. The starting point for the structure-activity relationship (SAR) studies was the potent and selective competitive antagonists D-AP5 and D-AP7. A decision was made to incorporate the requisite acidic amino acid backbone into various cyclic structures, with the hope that by decreasing the conformational mobility of these molecules we could learn more about the steric and spatial requirements for NMDA antagonist activity and improve their potency and activity following systemic administration. Bioisosteric replacements with reduced polarity relative to the phosphonic acidic moiety, such as the tetrazole group were also explored. These efforts led to the discovery of a series of 4-tetrazolylalkyl substituted piperidine-2-carboxylic acids, exemplified by LY233053, along with a series of 6-substituted decahydroisoquinoline-3-carboxylic acids, exemplified by LY274614 and LY233536. The synthesis and SARs of these compounds will be discussed, along with aspects of molecular modelling for the NMDA receptor.

1992

2/AB/3 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15167287 PASCAL No.: 01-0331583
Analysis of weak UV-absorbing pharmaceutical drug substances using ce with condensation nucleation light-scattering detection
LYTLE Michelle L; MAGNUSSON Lars-Erik; WEI GUO; KOROPCHAK John A; RISLEY Donald S
Eli Lilly and Co., Lilly Corporate Center, Drop 6414, Indianapolis, Indiana 46285, United States; Department of Chemistry and Biochemistry, Southern Illinois University, Carbondale, Illinois 62901, United States
Journal: LC GC North America, 2001, 19 (6) 624-631 (5 p.)
Language: English
The authors developed new analytical methodology to determine three pharmaceutical drug substances - LY354740, LY293558, and LY235959 -using

capillary electrophoresis (CE) with condensation nucleation light-scattering detection. This CE-condensation nucleation light-scattering detection system can perform trace analysis for these drug substances, which lack sufficient ultraviolet chromophores. The authors obtained acceptable levels of precision, linearity, and limit of detection for these compounds using the CE-condensation nucleation light-scattering detection system.

2/AB/4 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14827759 PASCAL No.: 00-0510834
(Tetrazoyl- SUP 1 SUP 1 C)LY202157 synthesis for in vivo studies of the NMDA receptor channel complex
PONCHANT M; GALEA H; BOTTLAENDER M; COULON C; FUSEAU C; OTTAVIANI M; CROUZEL C
Service Hospitalier Frederic Joliot, Departement de Recherche Medicale CEA / DSV 4 place du general Leclerc, 91406 Orsay, France
Journal: Journal of labelled compounds & radiopharmaceuticals, 2000, 43 (13) 1311-1320
Language: English
(Tetrazoyl- SUP 1 SUP 1 C)LY202157 8 was prepared via a three step synthesis from ethyl (3S,4aR,6S,8aR)-6-bromomethyl-2-methoxycarbonyl-1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylate 4. This bromo precursor was reacted with (SUP 1 SUP 1 C)hydrogen cyanide affording the corresponding (SUP 1 SUP 1 C)nitrile. Conversion to the tetrazole was achieved by treatment with azidotributyltin followed by hydrolysis with 6N hydrochloric acid at 200 Degree C. After HPLC purification and analytical HPLC control, more than 370 MBq (10 mCi) of (tetrazoyl- SUP 1 SUP 1 C) LY202157 were obtained after an overall 60 minute synthesis time with 38% yield (EOB) and specific activity of 25.9 GBq/ mu mol (700 mCi/ mu mol). Ex vivo biological studies showed that the (tetrazoyl- SUP 1 SUP 1 C) LY202157 did not cross the brain blood barrier.

2/AB/5 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

13896976 PASCAL No.: 99-0076871
Synthese de radioligands marques au brome-76 et au carbone-11 pour l'etude des recepteurs N-Methyl-D-Aspartate par Tomographie d'Emission de Positons
(Synthesis of bromine-76 and carbon-11 labelled radioligands for studying the N-Methyl-D-Aspartate receptors using Positron Emission Tomography)
GALEA Helene; LASNE Marie-Claire, dir
Universite de Caen, Caen, Francee
Univ.: Universite de Caen. Caen. FRA Degree: Th. doct.
1998-04; 1998 170 p.
Language: French Summary Language: French; English
Les recepteurs N-Methyl-D-Aspartate (NMDA) sont impliques dans diverses pathologies du systeme nerveux central telles que les accidents vasculaires cerebraux, les traumatismes, l'epilepsie et les maladies de Parkinson et d'Huntington. Malgre l'interet que represente la possibilite de visualiser in vivo les recepteurs NMDA par Tomographie d'Emission de Positons (TEP), aucun radioligand exploitable n'existe a ce jour. Nous avons prepare et teste les analogues radiomarques de deux antagonistes des recepteurs NMDA :

le (SUP 7 SUP 6 Br)RPR104632 (acide 6,8-dichloro-3,4-dihydro-2-(3-(SUP 7 SUP 6 Br)bromobenzyl)-2H-1,2,4-benzothiadiazine-1,1-dioxyde-3-carboxylique) et le (SUP 1 SUP 1 C)LY202157 (acide (SUP 1 SUP 1 C)-(3S,4aR,6S,8aR)-6-(1H-tetrazol-5-ylmethyl)-1,2,3,4,4a,5,6,7,8,8a-decahyd roisoquinoleine-3-carboxylique). Le (SUP 7 SUP 6 Br)RPR104632 a ete prepare avec un rendement de 7,7% en moyenne (non corrige de la decroissance) pour un temps de synthese de 150-180 minutes a partir du (SUP 7 SUP 6 Br)bromure d'ammonium. Le (SUP 1 SUP 1 C)LY202157 a ete obtenu avec un rendement moyen de 8,1% (corrige de la decroissance) pour un temps de synthese total d'environ 60 minutes a partir du (SUP 1 SUP 1 C)methane. La cinetique cerebrale des deux composes radiomarques a ete etudiee chez le rat. Leur passage de la barriere hemato-encephalique est tres mauvais et par consequent les concentrations dans le cerveau sont tres faibles. En conclusion, aucun de ces deux composes ne peut etre exploite comme radioligand pour la TEP.

2/AB/6 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

13455479 PASCAL No.: 98-0150844
The separation of enantiomers by countercurrent capillary electrophoresis using the macrocyclic antibiotic A82846B
REILLY J; RISLEY D S
Lilly Research Centre Ltd., Eli Lilly and Co., Erl Wood Manor, Windlesham, Surrey, GU20 6PH, United Kingdom; Lilly Research Laboratories, Pharmaceutical Sciences Division. Eli Lilly and Co., Lilly Corporate Center , Indianapolis, Indiana 46285, United States
Journal: LC GC, 1998, 16 (2) 170-178 (5 p.)
Language: English
The authors evaluated the macrocyclic antibiotic A82846B as a chiral selector by contrecurrent capillary electrophoresis using three dansyl aminoacids, three antiinflammatory compounds, and the 2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl)propionic acid antagonist LY215490 as the test analytes. They evaluated the chiral selectivity of A82846B as a function of the run buffer pH and antibiotic concentration. After optimizing variations of these parameters, the macrocyclic antibiotic A82846B provided high resolutions af all enantiomers for the compounds tested in this study. The detection and enantioseparation of LY215490, a compound lacking an adequate UV chromophore, demonstrated the practicality of the countercurrent process using A82846B, a chiral selector possessing a strong UV chromophore

2/AB/7 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

12400161 PASCAL No.: 96-0049032

(3SR,4aRS,6SR,8aRS)-6-(1H-Tetrazol-5-yl)decahydroisoquinoline-3-carboxylic acid, a novel, competitive, systemically active NMDA and AMPA receptor antagonist
ORNSTEIN P L; ARNOLD M B; ALLEN N K; LEANDER J D; TIZZANO J P; LODGE D; SCHOEPP D D
Lilly Corporate Center, Lilly Research Laboratories, Indianapolis IN 46285, USA
Journal: Journal of medicinal chemistry, 1995, 38 (25) 4885-4890

Language: English

We report the synthesis and characterization of 6 (LY246492), which is a competitive N-methyl-D-aspartate (NMDA) and 2-amino-3-(3-hydroxy-5-methylis oxazol-4-yl)propanoic acid (AMPA) receptor antagonist. Tetrazole-substitute d amino acid 6 was prepared in four steps from the recently described aldehyde 7. The optical isomers (-)-6 and (+)-6 were obtained from the same sequence of reactions using the corresponding isomers of 7. The compound displaces both NMDA and AMPA receptor binding and antagonizes depolarizations in cortical slices evoked by both NMDA and AMPA. In mice and pigeons, the compound showed antagonism of responses mediated through NMDA and AMPA receptors. Using the resolved optical isomers of 6, both NMDA and AMPA antagonist activities were found to reside in a single isomer, (-).6.

2/AB/8 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

12288750 PASCAL No.: 95-0520934

In vitro and in vivo antagonism of AMPA receptor activation by (3S,4aR,6R,8aR)-6-(2-(1(2)H-tetrazole-5-yl)ethyl)decahydroisoquinoline-3-ca rboxylic acid

SCHOEPP D D; LODGE D; BLEAKMAN D; LEANDER J D; TIZZANO J P; WRIGHT R A; PALMER A J; SALHOFF C R; ORNSTEIN P L

Elli Lilly and Co., Lilly Corporate Center, Lilly Research Laboratories, Indianapolis IN 46285, USA

Journal: Neuropharmacology, 1995, 34 (9) 1159-1168

Language: English

The in vitro and in vivo pharmacology of a structurally novel competitive antagonist for the alpha -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) subtype of excitatory amino acid receptors is described. LY215490, (+-)(6-(2-(1-H-tetrazol-5-yl)ethyl)decahydroisoquinoline-3-carb oxylic acid), was shown to displace selectively SUP 3 H-AMPA and SUP 3 H-6-cyano-7-nitro-quinoxaline-2,3-dione (SUP 3 H-CNQX) binding to rat brain membranes. LY215490 potently antagonized quisqualate-and AMPA-induced depolarizations of rat cortical slices in a competitive manner, while requiring higher concentrations to antagonize the effects of N-methyl-D-aspartate (NMDA) and kainate. In slices of rat hippocampus, LY215490 also selectively antagonized AMPA-evoked release of SUP 3 H-norepinephrine. These AMPA receptor activities were due to the (-) isomer of the compound, (3S,4aR,6R,8aR)-6-(2-(1(2)H-tetrazole-5-yl)ethyl)decahydro isoquinoline-3-carboxylic acid (LY293558). LY215490 was centrally active following parenteral administration in mice as demonstrated by protection versus maximal electroshock seizures and decreases in spontaneous motor activity. LY215490 (its active isomer being LY293558) represents a novel pharmacological agent for in vitro and in vivo studies of AMPA receptor function in the CNS.

2/AB/9 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal

11075285 PASCAL No.: 93-0582298

(3SR,4aRS,6RS,8aRS)-6-(2-(1H-tetrazol-5-yl)ethyl)decahydroisoquinoline-3-ca rboxylic acid : a structurally novel, systemically active, competitive AMPA receptor antagonist

ORNSTEIN P L; ARNOLD M B; AUGENSTEIN N K; LODGE D; LEANDER J D; SCHOEPP D D

Eli Lilly & Co., Lilly Research Laboratories, Indianapolis IN 46285, USA

Journal: Journal of medicinal chemistry, 1993, 36 (14) 2046-2048

Language: English

2/AB/10 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

10495784 PASCAL No.: 93-0005035
6-substituted decahydroisoquinoline-3-carboxylic acids as potent and selective conformationally constrained NMDA receptor antagonists
ORNSTEIN P L; SCHOEPP D D; ARNOLD M B; AUGENSTEIN N K; LODGE D; MILLAR J D; CHAMBERS J; CAMPBELL J; PASCHAL J W; ZIMMERMAN D M; LEANDER J D
Eli Lilly Co., Lilly Research Laboratories, Indianapolis IN 46285, USA
Journal: Journal of medicinal chemistry, 1992, 35 (19) 3547-3560
Language: English

2/AB/11 (Item 1 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx

02611017 WPI Acc No: 96-299884/30
Treating neurological disorders or producing analgesia - using 6-(tetrazolyl or isoxazolyl)-decahydroisoquinoline -3-carboxylic acid derivs. having excitatory aminoacid receptor antagonist activity
Patent Assignee: (ELIL) LILLY & CO ELI
Author (Inventor): ORNSTEIN P L
Patent (basic)

Patent No	Kind	Date	Examiner	Field of Search
US 5527810	A	960618 (BASIC)		514/307; 546/144; 546/147

Derwent Week (Basic): 9630
Priority Data: US 255590 (940608)
Applications: US 255590 (940608)
Derwent Class: B02
Int Pat Class: A01N-043/42
Number of Patents: 001
Number of Countries: 001
Number of Cited Patents: 004
Number of Cited Literature References: 051
Number of Citing Patents: 002

2/AB/12 (Item 2 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx

01396438 WPI Acc No: 94-332369/41
New 6-tetrazolyl or isoxazolyl-decahydro-isoquinoline-3-carboxylic acid derivs - useful as NMDA and AMPA excitatory aminoacid receptor antagonists for treating eg neurological disorders and pain
Patent Assignee: (ELIL) LILLY & CO ELI
Author (Inventor): ORNSTEIN P L
Patent (basic)

Patent No	Kind	Date	Examiner	Field of Search
US 5356902	A	941018 (BASIC)		514/307; 546/144; 546/147

Derwent Week (Basic): 9441
Priority Data: US 972679 (921106)
Applications: US 972679 (921106)
Derwent Class: B02
Int Pat Class: A01N-043/42
Number of Patents: 001
Number of Countries: 001
Number of Cited Patents: 002

Number of Cited Literature References: 063
Number of Citing Patents: 009

2/AB/13 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

015032356
WPI Acc No: 2003-092873/200308
XRAM Acc No: C03-023137
New method of treating or preventing a neurological disorder e.g. Fragile X, autism, mental retardation, schizophrenia and Downs' syndrome comprises administering Group I metabotropic glutamate receptor (mGluR) antagonist
Patent Assignee: UNIV BROWN RES FOUND (UYBR-N)
Inventor: BEAR M F; HUBER K M
Number of Countries: 100 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200278745	A2	20021010	WO 2002US10211	A	20020402	200308	B

Priority Applications (No Type Date): US 2001280915 P 20010402
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200278745	A2	E	81	A61K-045/08	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

Abstract (Basic): WO 200278745 A2
Abstract (Basic):

NOVELTY - New method of treating, preventing or lessening the severity of a neurological disorder selected from Fragile X, autism, mental retardation, schizophrenia and Downs' syndrome comprises administering a Group I metabotropic glutamate receptor (mGluR) antagonist.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit (A) comprising at least one Group I mGluR antagonist, provided in single oral dosage form or as a transdermal patch with instructions (written and/or pictorial) describing the use of the kit, and optionally warnings of possible side effects and drug-drug or drug-food interactions.

ACTIVITY - Nootropic; Neuroleptic.

MECHANISM OF ACTION - Metabotropic glutamate receptor (mGluR) antagonist binder.

To examine the effect of metabotropic glutamate receptor (mGluR) activation on alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate receptor (AMPARs) expressed on the surface of hippocampal neurons, an acid-strip immunocytochemical staining protocol was used. Surface receptors on living cultured hippocampal neurons were labeled with antibodies directed against the extracellular N-terminus of the GluR1 subunit. The cells were treated with either (RS)-3,5-dihydroxyphenylglycine (DHPG) (50 microM, 5 minutes) or control medium and after various intervals, the remaining surface antibodies were stripped away with an acetic acid wash. The neurons were fixed and immunocytochemistry was done under membrane-permeabilizing conditions to detect antibodies bound to internalized AMPARs.

DHPG application for 5 minutes stimulated a greater than 2-fold increase in internalized GluR1 puncta that was observed as early as 15 minutes after treatment onset (puncta per 10 microl of dendrite, control, 0.62:1+/-0.09, n=65 cells; DHPG, 1.44:1+/-0.17, n=60 cells; p less than 0.0002) and persisted for at least 1 hour (control, 0.58:1+/-0.08, n=42 cells; DHPG, 1.14+/-0.15, n=38 cells). The increased internalization of GluR1 was a specific consequence of activating groups I mGluR, as it was completely blocked by the mGluR antagonist LY344545. In contrast, the N-methyl-D-aspartate receptors (NMDAR) antagonist 2-amino-5-phosphonovaleric acid (APV) (50 microM) had no effect (control, 0.74+/-0.19, n=7; DHPG, 1.49+/-0.22, n=10; DHPG+APV, 1.51+/-0.3, n=10).

USE - For treating, preventing or lessening the severity of a neurological disorder such as Fragile X, autism, mental retardation, schizophrenia and Down's syndrome. The kit may be used for conducting a pharmaceutical business by marketing to healthcare providers the benefits of using the kit; providing instruction material to patients or physicians for using the kit; determining an appropriate dosage of an mGluR antagonist to treat neurological disorder in a patients by conducting therapeutic profiling of formulations of the mGluR antagonist for efficacy and toxicity in animals; providing a distribution network for selling a kit or the formulation, by licensing, to a third party, the rights for further development and sale of the mGluR antagonist for treating neurological disorder or additionally providing a sales group for marketing the preparation to healthcare providers (all claimed).

ADVANTAGE - The mGluR antagonist has an ED50 for mGluR5 antagonism of at least 10 times less than that for mGluR1 and at least 100 times less than the ED50 for antagonism of ionotropic glutamate receptors. The mGluR antagonist has an ED50 of at most1 microM (preferably at most100 nM) and has a therapeutic index (TI) of at least10 (preferably at least100) (all claimed).

pp; 81 DwgNo 0/9

2/AB/14 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

014997879
WPI Acc No: 2003-058394/200305
XRAM Acc No: C03-014889

Treatment of animal that has suffered or having a risk of damage to cerebrospinal tissue involves injecting cerebrospinal perfusion fluid between two catheters to create flow pathway and maintaining the flow

Patent Assignee: NEURON THERAPEUTICS INC (NEUR-N)
Inventor: FRAZER G D; HESSON D P; ROSS D
Number of Countries: 099 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200278670	A1	20021010	WO 2002US5885	A	20020228	200305	B

Priority Applications (No Type Date): US 2001798880 A 20010302
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200278670	A1	E	28	A61K-009/107	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

Abstract (Basic): WO 200278670 A1
Abstract (Basic):
NOVELTY - Treatment of an animal that has suffered or has an indication of creating a risk of damage to cerebrospinal tissue is new.
DETAILED DESCRIPTION - Treatment of an animal that has suffered or has an indication of creating a risk of damage to cerebrospinal tissue involves:
(a) Injecting cerebrospinal perfusion fluid (containing a neuroprotectant) into a first catheter into the cerebrospinal pathway;
(b) Withdrawing fluid at a second catheter into the cerebrospinal pathway to create a flow pathway between the two catheters; and
(c) Maintaining the flow for a period of time adapted to perfuse an affected tissue
ACTIVITY - Cerebroprotective; Tranquilizer; Vulnerary; Nootropic; Neuroprotective; Hemostatic; Vasotropic.
MECHANISM OF ACTION - None given.
USE - For treatment of an animal (preferably human) that has suffered or has an indication of creating a risk of damage to cerebrospinal tissue, such as stroke, a neurodegenerative disease, trauma, Alzheimer's disease, and multiple sclerosis (all claimed) e.g. for the treatment of amyotrophic lateral sclerosis, traumatic brain injury (TBI), brain hemorrhage, spinal cord traumatic injury, and ischemia caused by surgical intervention and central nervous system, ischemic or chemical injury. Also useful to remove neurotoxic by-products while optionally providing oxygen, glucose, electrolytes and essential amino acids into the neural tissue; and also to supply nutrients, and remove toxic metabolic waste.
ADVANTAGE - Central nervous system (CNS) perfusion of the neuroprotectant allows control of both dose and duration of exposure of the agent compared to other routes of administration such as oral, intravenous or systemic administrations. The method allows the circulation of the neuroprotectant throughout the
neuraxis, thus exposing nervous system tissue to the agent in a more uniformly and continuously controlled dose; while maintaining the neuroprotectant within a narrow concentration range, avoiding the necessity of high bolus concentration over time. The method also allows exposure of nervous system to the agent for extended period of time, such as days, if necessary; and minimizes the amount of drug necessary to achieve a therapeutic effect. The method allows, both the supply of nutrients and the removal of metabolic waste, at the same time.
pp; 28 DwgNo 0/1

2/AB/15 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

013653840
WPI Acc No: 2001-138052/200114
XRAM Acc No: C01-040599
Selective iGlurR5 antagonists useful for treating migraine, Alzheimer's disease, depression and cardiac arrest
Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: BLEAKMAN D; CHAPPELL A S; FILLA S A; JOHNSON K W; ORNSTEIN P L
Number of Countries: 095 Number of Patents: 010
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200101972	A2	20010111	WO 2000US16297	A	20000627	200114	B
AU 200058732	A	20010122	AU 200058732	A	20000627	200125	
NO 200106246	A	20020304	WO 2000US16297	A	20000627	200223	
			NO 20016246	A	20011219		
BR 200012175	A	20020305	BR 200012175	A	20000627	200225	

			WO 2000US16297	A	20000627		
EP 1200073	A2	20020502	EP 2000944671	A	20000627	200236	
			WO 2000US16297	A	20000627		
KR 2002024300	A	20020329	KR 2002700138	A	20020105	200265	
CN 1359289	A	20020717	CN 2000809688	A	20000627	200268	
JP 2003503449	W	20030128	WO 2000US16297	A	20000627	200309	
			JP 2001507466	A	20000627		
CZ 200104488	A3	20030115	WO 2000US16297	A	20000627	200309	
			CZ 20014488	A	20000627		
HU 200202253	A2	20021128	WO 2000US16297	A	20000627	200309	
			HU 20022253	A	20000627		

Priority Applications (No Type Date): US 99151165 P 19990827; US 99142485 P 19990706

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200101972	A2	E	33	A61K-031/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200058732	A		A61K-031/00	Based on patent WO 200101972
NO 200106246	A		A61K-000/00	
BR 200012175	A		A61K-031/00	Based on patent WO 200101972
EP 1200073	A2	E	A61K-031/00	Based on patent WO 200101972

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

KR 2002024300	A		A61K-031/4725	
CN 1359289	A		A61K-031/00	
JP 2003503449	W	53	A61K-045/00	Based on patent WO 200101972
CZ 200104488	A3		A61K-031/4745	Based on patent WO 200101972
HU 200202253	A2		A61K-031/00	Based on patent WO 200101972

Abstract (Basic): WO 200101972 A2

Abstract (Basic):

NOVELTY - Treating migraine comprises administration of a selective iGluR5 receptor antagonist or its salt.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a method of treating dural protein extravasation comprising administration of a selective iGluR5 receptor antagonist; and

(2) novel decahydroisoquinoline compounds of formula (I).

R1, R2=H, 1-20C alkyl, 2-6C alkenyl, 1-6C alkylaryl, 1-6C alkyl-3-10C cycloalkyl, 1-6C alkyl-N,N-1-6C dialkylamine, 1-6C alkyl-pyrrolidine, 1-6C alkyl-piperidine, or 1-6C alkyl-morpholine.

ACTIVITY - Cerebroprotective; Cardiant; Nootropic; Neuroprotective; Anticonvulsant; Antidepressant; Tranquilizer; Neuroleptic; Analgesic; Antimigraine.

In an animal model of dural protein extravasation, 3S, 4aR, 6S, 8aR-6-((((1H-**tetrazole**-5-yl)methyl)oxy)methyl)-1,2,3,4,4a,5,6,7,8,8a-**decahydroisoquinoline-3-carboxylic** acid (III) exhibited an ID50 of 15 ng/kg in the rat, for inhibition of protein extravasation, an exemplary function of the neuronal mechanism of migraine.

MECHANISM OF ACTION - iGluR5-Antagonist.

USE - The methods and compounds are useful for treating or preventing a neurological disorder, or neurodegenerative condition such as stroke, cerebral ischemia, perinatal hypoxia, cardiac arrest, Alzheimer's disease, Huntington's chorea, AIDS-induced dementia, amyotrophic lateral sclerosis, idiopathic and drug-induced Parkinson's disease, ocular damage and retinopathy, muscular spasticity, drug

tolerance and withdrawal, brain edema, convulsive disorders including epilepsy, tardive dyskinesia, schizophrenia, mania and acute and chronic pain states.
pp; 33 DwgNo 0/0

2/AB/16 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI

013023117
WPI Acc No: 2000-194968/200017
XRAM Acc No: C00-060376
Use of inhibitor of interaction of glutamate with alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionate or kainate receptor complex for treatment of demyelinating disorders e.g. multiple sclerosis
Patent Assignee: EISAI CO LTD (EISA)
Inventor: SMITH T; TURSKI L
Number of Countries: 021 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200001376	A2	20000113	WO 99GB2112	A	19990702	200017	B
EP 1100504	A2	20010523	EP 99929545	A	19990702	200130	
			WO 99GB2112	A	19990702		
JP 2002519373	W	20020702	WO 99GB2112	A	19990702	200246	
			JP 2000557823	A	19990702		

Priority Applications (No Type Date): GB 9824393 A 19981106; GB 9814380 A 19980702
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200001376	A2	E	104	A61K-031/00	
Designated States (National): JP US					
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
EP 1100504	A2	E		A61K-031/498	Based on patent WO 200001376
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002519373	W		130	A61K-045/06	Based on patent WO 200001376

Abstract (Basic): WO 200001376 A2
Abstract (Basic):
NOVELTY - Use of an inhibitor (I) of the interaction of glutamate with the alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionate (AMPA) receptor complex and of the interaction of glutamate with the kainate receptor complex in the manufacture of a medicament for treatment of demyelinating disorder (DMD) is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) use of an inhibitor of interaction of glutamate with an AMPA receptor for treatment of demyelinating disorders;
(2) use of an inhibitor of interaction of glutamate with the kainate receptor for treatment of demyelinating disorders.
ACTIVITY - Neuroprotective; immunosuppressive.
The figure shows the effect of the AMPA receptor antagonist NBQX on severity of paralysis during experimental allergic encephalomyelitis (EAE) in rats, at a dose of 30 mg/kg twice daily.
MECHANISM OF ACTION - Glutamate-AMPA and/or kainate receptor complex interaction inhibitors.
USE - For treatment of DMD such as acute disseminated encephalomyelitis, acute demyelinating polyneuropathy (Guillain Barre syndrome), chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, Marchifava-Bignami disease, central pontine myelinolysis, Devic syndrome, Balo disease, human immunodeficiency virus (HIV)- or

human T-cell leukemia virus (HTLV)-myelopathy, progressive multifocal leucoencephalopathy or a secondary demyelinating disorder, particularly CNS lupus erythematodes, polyarteriitis nodosa, Sjogren syndrome, sarcoidosis or isolated cerebral vasculitis (all claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the effect of the AMPA receptor antagonist NBQX on severity of paralysis during EAE in rats, at a dose of 30 mg/kg twice daily.

pp; 104 DwgNo 1/8

2/AB/17 (Item 5 from file: 351)
DIALOG(R)File 351:Derwent WPI

012140539
WPI Acc No: 1998-557451/199847
XRAM Acc No: C98-166883
Treatment of pain - with glur-five receptor antagonists and new decahydroisoquinoline antagonists of this class
Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: BLEAKMAN D; HELTON D R; IYENGAR S; LODGE D; ORNSTEIN P L; SMRITI I
Number of Countries: 083 Number of Patents: 014
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9845270	A1	19981015	WO 98US6905	A	19980406	199847	B
AU 9869555	A	19981030	AU 9869555	A	19980406	199911	
NO 9904850	A	19991005	WO 98US6905	A	19980406	200004	
			NO 994850	A	19991005		
EP 980358	A1	20000223	EP 98915346	A	19980406	200015	
			WO 98US6905	A	19980406		
CZ 9903541	A3	20000412	WO 98US6905	A	19980406	200026	
			CZ 993541	A	19980406		
BR 9809071	A	20000801	BR 989071	A	19980406	200043	
			WO 98US6905	A	19980406		
CN 1259126	A	20000705	CN 98805687	A	19980406	200052	
NZ 337827	A	20001222	NZ 337827	A	19980406	200104	
			WO 98US6905	A	19980406		
MX 9909140	A1	20000101	MX 999140	A	19991006	200115	
HU 200002030	A2	20010428	WO 98US6905	A	19980406	200131	
			HU 20002030	A	19980406		
US 6242462	B1	20010605	US 9742795	A	19970407	200133	
			WO 98US6905	A	19980406		
			US 2000402174	A	20000222		
AU 734657	B	20010621	AU 9869555	A	19980406	200141	
KR 2001006075	A	20010115	KR 99709153	A	19991006	200151	
JP 2001521505	W	20011106	JP 98542127	A	19980406	200203	
			WO 98US6905	A	19980406		

Priority Applications (No Type Date): US 9742795 P 19970407; US 2000402174 A 20000222
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9845270	A1	E	19	C07D-217/06	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9869555	A		C07D-217/06	Based on patent WO 9845270
NO 9904850	A		C07D-217/16	
EP 980358	A1	E	C07D-217/06	Based on patent WO 9845270

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI

CZ 9903541	A3		C07D-217/06	Based on patent WO 9845270
BR 9809071	A		C07D-217/06	Based on patent WO 9845270
CN 1259126	A		C07D-217/06	
NZ 337827	A		A61K-031/47	Based on patent WO 9845270
MX 9909140	A1		C07D-217/06	
HU 200002030	A2		C07D-217/06	Based on patent WO 9845270
US 6242462	B1		A61K-031/47	Provisional application US 9742795 Based on patent WO 9845270
AU 734657	B		C07D-217/06	Previous Publ. patent AU 9869555 Based on patent WO 9845270
KR 2001006075	A		C07D-217/06	
JP 2001521505	W	16	A61K-045/00	Based on patent WO 9845270

Abstract (Basic): WO 9845270 A

Mammalian pain is treated by administration of a selective Glu R5 receptor antagonist. The preferred antagonists are (i) 3SR, 4aRS, 6SR, 8aRS-6-((((1H-**tetrazol**-5-yl)methyl)oxy)-methyl)-1,2,3,4,4a,5,6,7,8,8a-**decahydroisoquinoline-3-carboxylic** acid; (ii) 3S, 4aR, 6S, 8aR-6-((((1H-**tetrazol**-5-yl)methyl)oxy)methyl) -methyl)-1,2,3,4,4a,5,6,7,8,8a-**decahydroisoquinoline-3-carboxylic** acid; (iii) 3SR, 4aRS, 6SR, 8aRS-6-(((4-carboxy)phenyl)methyl)- 1,2,3,4,4a,5,6,7,8,8a-**decahydroisoquinoline-3-carboxylic** acid; and (iv) 3S, 4aR, 6S, 8aR-(((4-carboxy)phenyl)methyl)- 1,2,3,4,4a,5,6,7,8,8a-**decahydroisoquinoline-3-carboxylic** acid. Compounds (ii) and (iv) are claimed as new, and may be made up into pharmaceutical compositions with suitable carriers.

Dwg.0/0

2/AB/18 (Item 6 from file: 351)
DIALOG(R)File 351:Derwent WPI

011534822
WPI Acc No: 1997-511303/199747
Related WPI Acc No: 1994-056413; 1995-138330; 1997-164018; 1997-319117; 1997-372117; 1997-548398
XRAM Acc No: C97-163142

New decahydro-isoquinoline derivatives - are excitatory amino acid receptor antagonists used to treat neurological disorders

Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: ARNOLD M B; AUGENSTEIN N K; LUNN W H W; ORNSTEIN P L; SCHOEPP D D
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 5670516	A	19970923	US 92939780	A	19920903	199747 B
			US 93111747	A	19930825	
			US 94343079	A	19941121	
			US 95456439	A	19950601	

Priority Applications (No Type Date): US 92939780 A 19920903; US 93111747 A 19930825; US 94343079 A 19941121; US 95456439 A 19950601
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5670516	A		45	C07D-215/14	Div ex application US 92939780 Div ex application US 93111747 Div ex application US 94343079 Div ex patent US 5284957 Div ex patent US 5399696

Abstract (Basic): US 5670516 A

Decahydroisoquinoline derivatives of formula (I) and their salts are new: R1 = H, 1-10C alkyl, aralkyl, alkoxycarbonyl or acyl; R2 = H, 1-6C alkyl, substituted alkyl, cycloalkyl or aralkyl; R3 = CO2H, SO3H, CONHSO2R8 or a group of formula (a)-(k); W = (CH2)n, S, SO or SO2; Y = CHR7, NR4, O, S, SO or SO2; Z = NR6, CHR7 or CH; or W + Y or Y + Z = HC=CH or C triple bond C; R4 = H, 1-4C alkyl, Ph or acyl; R5 = H, 1-4C alkyl, CF3, Ph, OH, amino, Br, I or Cl; R6 = acyl; R7 = H, 1-4C alkyl or optionally substituted Ph; R8 = 1-4C alkyl or tetrazol-5-yl; and n = 0-2; provided that: (i) when Y = NR4, O, S, SO or SO2, W = (CH2)n and Z = CHR7 or CH; and (ii) when W = S, SO or SO2, Y = CHR7, Z = CHR7 or CH, or Y + Z = HC=CH or C triple bond C; (iii) when W + Z = CH2, Y is not S; and (iv) when W + Y = HC=CH or C triple bond C, Z = CHR7.

2 Compounds are specifically claimed e.g: 6-(2-(1-(2)H-**tetrazole**-5-yl)ethyl)**decahydroisoquinoline-3-carboxylic** acid.

USE - (I) block the alpha -amino-3-hydroxy-5-methylisoxazole-4-propionic acid excitatory amino acid receptor and are used to treat neurological disorders comprising cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischaemia, spinal cord trauma, head trauma, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, AIDS induced dementia, muscular spasms, migraine headache, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycaemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug induced Parkinson's disease, anxiety, emesis, brain oedema, chronic pain or tardive dyskinesia. (I) are also useful as analgesics. The dosage of (I) is 0.01-20 (preferably 0.05-10, especially 0.1-5) mg/kg/day.

Dwg.0/0

2/AB/19 (Item 7 from file: 351)
DIALOG(R)File 351:Derwent WPI

011186093
WPI Acc No: 1997-164018/199715
Related WPI Acc No: 1994-056413; 1995-138330; 1997-319117; 1997-372117; 1997-511303; 1997-548398
XRAM Acc No: C97-052863

Prodn. of 6-(2-heterocyclyl ethyl) decahydro isoquinoline 3-carboxylic acid derivs. - by stereoselective redn. of heterocyclyl-ethylidene derivs.

Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: HUFF B
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 5606062	A	19970225	US 92939780	A	19920903	199715 B
			US 93111747	A	19930825	
			US 94343079	A	19941121	
			US 95457556	A	19950601	

Priority Applications (No Type Date): US 92939780 A 19920903; US 93111747 A 19930825; US 94343079 A 19941121; US 95457556 A 19950601
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5606062	A		44	C07D-217/16	Div ex application US 92939780 Div ex application US 93111747 Div ex application US 94343079 Div ex patent US 5284957 Div ex patent US 5399696

Abstract (Basic): US 5606062 A

Prodn. of (3S,4aR,6R,8aR)-6-(2-heterocyclyl ethyl)-decahydro-isoquinoline-**3-carboxylic** acid derivs. of formula (I) comprises stereoselectively reducing heterocyclyl-ethylidene derivs. of formula (II). J = 3-hydroxy-(4-R5)-5-isoxazolyl, 3-hydroxy-(5-R5)-4-isoxazolyl, 4-hydroxy-1,2,5-thiadiazol-3-yl, or opt. N-protected 1H-**tetrazol**-5-yl, 2H-**tetrazol**-5-yl, (5-R5)-2H-1,2,4-triazol-3-yl, (5-R5)-4H-1,2,4-triazol-3-yl, (5-R5)-1H-1,2,4-triazol-3-yl, (5-R5)-2H-1,2,3-triazol-4-yl or (5-R5)-3H-1,2,3-triazol-4-yl; R5 = H, 1-4C alkyl, CF3, Ph, OH, NH2, Br, I or Cl; R9 = alkoxycarbonyl or acyl; and R10 = 1-6C alkyl or Ph.

USE - (I) are selective AMPA receptor antagonists used for treating neurological disorders, e.g. cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischaemia, spinal cord trauma, head trauma, Alzheimer' s Disease, Huntington' s Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycaemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain oedema, chronic pain or tardive dyskinesia. (I) are also used as analgesic agents.

Dwg.0/0

2/AB/20 (Item 8 from file: 351)
DIALOG(R)File 351:Derwent WPI

010802931
WPI Acc No: 1996-299884/199630
Related WPI Acc No: 1994-332369
XRAM Acc No: C96-095282

Treating neurological disorders or producing analgesia - using 6-(**tetrazolyl** or isoxazolyl)-**decahydroisoquinoline -3-carboxylic** acid derivs. having excitatory aminoacid receptor antagonist activity

Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: ORNSTEIN P L
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5527810	A	19960618	US 92972679	A	19921106	199630	B
			US 94255590	A	19940608		

Priority Applications (No Type Date): US 92972679 A 19921106; US 94255590 A 19940608

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5527810	A		17	A01N-043/42	Div ex application US 92972679
					Div ex patent US 5356902

Abstract (Basic): US 5527810 A

Treating neurological disorders or producing analgesia comprises admin. of a decahydroisoquinoline deriv. of formula (I) or its salt: R1 = H, 1-10C alkyl, aralkyl, alkoxycarbonyl, acyl or aryloxycarbonyl; R2 = H, 1-6C alkyl, substd. alkyl, cycloalkyl or aralkyl; R3 = a gp. of formula (a)-(c); R4 = H, 1-4C alkyl, CF3, Ph, Br, I or Cl.

USE - (I) are excitatory aminoacid receptor antagonists specifically AMPA and NMDA receptor antagonists used to treat neurological disorders e.g. cerebral deficits subsequent to cardiac

bypass surgery and grafting, stroke, cerebral ischaemia, spinal cord trauma, head trauma, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycaemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's disease, anxiety, emesis, brain oedema, chronic pain or tardive dyskinesia.

(I) are also analgesics.

Dosage is 0.01-30 (esp. 0.1-20) mg/kg.

Dwg.0/0

2/AB/21 (Item 9 from file: 351)
DIALOG(R)File 351:Derwent WPI

010064658
WPI Acc No: 1994-332369/199441
Related WPI Acc No: 1996-299884
XRAM Acc No: C94-151167

New 6-**tetrazolyl** or isoxazolyl-decahydro-**isoquinoline-3-carboxylic** acid derivs - useful as NMDA and AMPA excitatory aminoacid receptor antagonists for treating eg neurological disorders and pain

Patent Assignee: LILLY & CO ELI (ELIL)
Inventor: ORNSTEIN P L
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5356902	A	19941018	US 92972679	A	19921106	199441	B

Priority Applications (No Type Date): US 92972679 A 19921106
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5356902	A		17	A01N-043/42	

Abstract (Basic): US 5356902 A

Isoquinoline derivs. of formula (I) and their salts are new. R1 = H, 1-10C alkyl, arylalkyl, alkoxycarbonyl, aryloxycarbonyl, or acyl; R2 = H, 1-6C alkyl, substd. alkyl, cycloalkyl or arylalkyl; R3 = 1H-tetrazol-5-yl, 2H-tetrazol-5-yl or 3-hydroxy-4-R4-isoxazol-5-yl; R4 = H, 1-4C alkyl, CF3, Br, I, Cl or phenyl; acyl = HCO or 2-7C alkylcarbonyl; substd. alkyl = 1-6C alkyl substd. by 1 or more of OH, F, Cl, Br or I; cycloalkyl = 3-7C.

USE - (I) are antagonists of the alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and N-methyl-D-aspartate (NMDA) excitatory amino acid receptors. They are useful for treating neurological disorders linked to these excitatory aminoacid receptors, e.g., cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischaemia, spinal cord trauma, head trauma, Alzheimer's disease, Huntington's' chorea, amyotrophic lateral sclerosis, AIDS induced dementia, perinatal hypoxia, cardiac arrest, hypoglycaemic neuronal damage, ocular damage and retinopathy and idiopathic and drug induced Parkinson's disease. (I) are also useful as analgesics; and for treating disorders related to glutamate dysfunction, e.g. muscular spasm, convulsions, migraine, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain oedema, chronic pain and tardive dyskinesia.

Dwg.0/0

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